silk hats, the measured tread, the grave nod of the head—at very least with ambulation, continence, and mental clarity—features which are lacking as death approaches. Near the end of life some old people become undignified, remove their clothing in public, and revile their dear ones with obscenities. Others lose self-control and become irritable, demanding, and selfish; refuse to be left alone; moan repetitively; ceaselessly ask for drinks; or demand to be taken to the lavatory, do nothing, then wet themselves. These anxiety symptoms are hard for relatives to bear; and many have confided to me that the last months of a loved parent's life were the worst they had ever experienced.

These situations test to the utmost the doctor's capacity to treat the irremediable. He must listen, sympathize, reassure' explain. The relatives require our ears and our time, but the doctor can also give practical help by arranging day hospital care or short-term admission.

Conclusion

Much of medical work is concentrated on the final months or year of life. The curative role of the doctor is being attenuated. But equal or greater professional satisfaction can be found by the skilled and perceptive treatment of "the irremediable."

Occasional Survey

Surgery in Management of Patients with Leukaemia

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Summary

Though leukaemia is not a "surgical" disease, the need for surgery in patients with leukaemia is increasing. Acute surgical problems in such patients present diagnostic difficulties, and accepted surgical principles do not necessarily apply in patients with very abnormal haematological and immunological features. The improved prognosis in some types of leukaemia means that elective surgical procedures, which formerly would not have been considered, may now be applicable just as they would be in patients with non-malignant conditions.

Recent advances in the management of the leukaemias include several surgical procedures—for example, to facilitate intravenous or intrathecal therapy. Splenectomy is of value in chronic lymphocytic leukaemia when the correct indications are present, while early elective splenectomy, when no classical indications are present, may have a useful role in the management of patients with chronic granulocytic leukaemia.

Introduction

Leukaemia has long seemed an example of a malignant disease where surgery has little place. The diagnosis is established without resort to operation. While laparotomy for staging purposes has a role in Hodgkin's disease,[1] and possibly in other malignant lymphomas,[2] such investigation seems needless in leukaemia, where the disease appears to affect from the outset all those parts of the body which are freely accessible from the vascular system. Leukaemia is certainly not curable by surgery, while the existence of reasonably effective medical treatment does not encourage an investigative surgical approach. Furthermore, thrombocytopenia and neutropenia, with enhanced risks of haemorrhage and infection, often make the patient with leukaemia an unattractive surgical proposition. Not surprisingly, surgical intervention in leukaemia patients has generally been restricted to urgent procedures, such as the incision of abscesses or appendicectomy for intercurrent acute appendicitis. In the recent past elective surgery even with good indications was often denied to leukaemic patients, particularly those with any form of acute leukaemia, since before the advent of effective antileukaemic therapy the median survival in these diseases was less than three months for both children and adults.[3]

Advances in the treatment of the leukaemias are altering this picture. In some cases improvements in prognosis have made the indications for elective surgery in a leukaemia patient almost identical with those for the same operation in a patient without leukaemia. Some facets of the medical treatment of the leukaemias can be greatly facilitated or their applicability broadened or their effects improved by various surgical procedures.

Surgery as Part of Initial Treatment

The untreated patient with acute leukaemia is often neutropenic and may have a serious infection at the time of diagnosis. Treatment for the infection is sometimes necessary before embarking on antileukaemic therapy, which in the initial stages usually worsens the neutropenia and may also cause immunosuppression. Surgical drainage of pus or extraction of an abscessed tooth are indicated as they would be in any other patient. If anything, the indications are stronger in the patient with leukaemia, since his ability to overcome infections, even with the aid of antibiotics, is reduced. Sometimes more drastic surgical procedures are indicated before other treatment is begun.

Case History.—A 55-year-old man presented with acute myeloid leukaemia. Eight years previously he had sustained an injury to his left hand. Despite a partial amputation he had a chronic osteomyelitis which discharged occasionally. On examination there were no clinical or radiological signs of activity and the sinus had healed. His leukaemia responded inadequately to initial chemotherapy. Before starting more intensive chemotherapy his

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skin and gut contents were rendered pathogen-free and he was placed in a plastic isolator (or "life island"). After his next course of chemotherapy had produced complete agranulocytosis his left hand became red and swollen. Severe cellulitis of hand and forearm was followed by axillary lymphadenitis and septicaemia with multiple lung abscesses. The patient died despite fresh granulocyte transfusions and massive antibiotic therapy.

To render drastic chemotherapy safe this man was placed in a pathogen-free environment after careful decontamination of his skin and gut. All these precautions were set at naught by the presence of a pathogenic organism within an old internal lesion. In retrospect it is seen that his old osteomyelitis should have been extirpated before therapy; its apparent quiescence should not have deterred this course of action. Standard surgical principles may not apply in situations which are highly atypical from an immunological or haematological standpoint.

Prophylactic Surgery during Remission

Improvement in prognosis consequent on advances in therapy has been most marked in the acute leukaemias, particularly lymphoblastic leukaemia in children.[4] Once a remission has been achieved by chemotherapy an adult has a life expectancy of several or many months, and a child may live several years or may actually be cured of the disease.[5] The early phase of a remission is a good time to extirpate actual or potential infected foci—for example, by clearing carious teeth, excising an ingrowing toenail or a pilonidal sinus, treating an anal fissure or fistula, or performing haemorrhoidectomy. In a subsequent relapse such lesions can be life-threatening, and at best their presence can hinder effective antileukaemic chemotherapy. While surgery during leukaemic relapse is often hazardous, the patient whose leukaemia is in remission is not at special risk. Thus the ability to secure remissions in the acute leukaemias makes some elective surgery not only feasible but also desirable.

Difficulties with Intravenous Therapy

The intravenous administration of drugs, blood, and platelet concentrates is an essential part of the management of patients with acute leukaemia. Even with care and skill it is not rare to exhaust temporarily the supply of suitable veins, especially in the obese and in children. One surgical approach to this problem is the insertion of a central venous catheter into the external jugular or cephalic vein via an infraclavicular incision.[6] The catheter is passed through the subcutaneous tissues and brought to the surface below the nipple, the long subcutaneous track ensuring that infection at the cutaneous entry site is remote from the great vessel. Mann and her colleagues[6] maintained the patency of their catheters with a portable clockwork infusion pump. We have used a slightly different technique, inserting a Pudenz cardiac catheter with radio-opaque tip and a non-return slit-valve into a tributary of the subclavian vein via an infraclavicular incision. The catheter is brought out at the costal margin and aseptically fixed to a plastic Guest's cannula. The slit-valve prevents reflux of blood and formation of thrombus within the cannula. Injections are made intermittently, and when not in use the assembly is filled with sterile water containing 0·9% benzyl alcohol as a bacteriostatic agent. (This solution is, in fact, the diluent supplied with cytosine arabinoside injection.) We have maintained these devices for up to three months without infection and have administered multiple courses of cytotoxic drugs by this route.

A more permanent alternative is the fashioning of an arteriovenous fistula, usually a window between the radial artery and a deep vein in the forearm. After a few weeks large pulsatile dilated veins appear in the cubital fossa; these are readily punctured and, owing to the rapid blood flow through them, will tolerate repeated injections of cytotoxic drugs without thrombosis. This type of internal shunt does not possess the infection hazard which would be associated with the use of a prosthetic external arteriovenous shunt in a leukaemic patient. When serious problems arise with intravenous therapy it is our practice to seek surgical help sooner rather than later, since repeated abortive venepunctures seriously demoralize both children and parents.

Orthopaedic Procedures

Osteolytic lesions with impending or actual pathological fracture are less common in the leukaemias than in myelomatosis. When such lesions occur in acute leukaemia they may be associated with poor control of the systemic disease and a very short life expectancy, in which case treatment is conservative. If, however, the prognosis appears to be one of months at least, internal fixation can relieve symptoms and restore mobility and should be seriously considered.

Case History.—A 45-year-old man with chronic myeloproliferative disease developed over a short period the picture of acute myeloid leukaemia. Multiple osteolytic deposits appeared in the pelvis and the subtrochanteric region of the right femur. Walking was painful and pathological fracture seemed imminent, so that weight-bearing was forbidden. He appeared likely to survive several months, so under the cover of fresh blood and platelet transfusion a pin and plate were inserted into the femur. Six units of blood were required for the operation but the postoperative course was uneventful. Biopsy material from the femur showed replacement of bone by leukaemic cells. The patient was walking in two weeks with very little pain. After postoperative radiotherapy to the bone lesions and systemic antileukaemic chemotherapy he was well enough to take an overseas trip, and lived for seven months after the operation, mostly at home with his family.

Though the orthopaedic operation probably did not affect the duration of this man's life there can be no doubt that it greatly improved its quality, and enabled him to leave hospital.

Subcutaneous C.S.F. Reservoirs

Involvement of the central nervous system is an increasing problem in children with acute leukaemia, and is attributable to improved survival and to other, possibly immunological, factors.[7] Longer survival in adults with acute leukaemia may be accompanied by a similar increase in nervous system leukaemia. Many therapeutic regimens, particularly in children, incorporate prophylaxis against central nervous system involvement.[8,9] Such prophylaxis usually includes irradiation and injections of antimetabolite drugs into the subarachnoid space. Five lumbar punctures during the three weeks over which radiotherapy is administered appear to be adequate.

Such a programme, however, is inadequate for the treatment of established meningeal leukaemia and there is a high relapse rate. Because meningeal leukaemia is such a serious disorder it is our policy in established cases to follow the initial radiotherapy and intrathecal therapy with weekly intrathecal injections of methotrexate, alternating with cytosine arabinoside, for a full year. Neither patients nor physicians appreciate repeated lumbar punctures carried out over weeks or months; this is particularly difficult with children. Lumbar puncture can be avoided by use of the subcutaneous cerebrospinal fluid reservoir described by Ommaya.[10,11] The small plastic reservoir is installed beneath the scalp and connected by a catheter to the lateral ventricle of the non-dominant (usually the right) cerebral hemisphere. Insertion of a reservoir involves the making of a single occipital or frontal burr-hole and is a minor neurosurgical procedure, usually

taking less than an hour. Use of a denervating scalp incision makes percutaneous puncture of the reservoir completely painless. With this simple device it is possible to treat established meningeal leukaemia very vigorously for an extended period with the minimum of discomfort or distress to the patient or his parents.[12]

Laparotomy in Leukaemia

Laparotomy is uncommon in patients with leukaemia and, of course, plays no part in the routine management of this group of diseases; nevertheless, it sometimes has to be performed. In patients with acute leukaemia in remission, or with either chronic granulocytic leukaemia or chronic lymphocytic leukaemia in good haematological control, abdominal symptoms and signs are by no means certain to be due to their primary disease or its treatment. It is, perhaps, wisest to assess such patients as if they did not have leukaemia at all and consider the clinical findings on their own merits, since affliction with leukaemia certainly carries no exemption from intercurrent unrelated surgical conditions of the abdominal contents. It is true that certain antileukaemic drugs can produce abdominal symptoms—for example, pain and constipation from vincristine, pancreatitis from asparaginase (rarely), and haematemesis due to corticosteroid drugs. In many cases, however, findings which would dictate laparotomy in a normal individual also justify surgical exploration in a patient with leukaemia.

In poorly controlled leukaemia of any type surgical assessment may be more difficult. Pain from splenic infarction or retroperitoneal haemorrhage may be correctly diagnosed and treated conservatively, but on occasion the surgeon's hand is forced, and the findings at laparotomy may be unexpected.

Case 1.—A man of 28 with acute myeloblastic leukaemia in relapse developed seemingly unequivocal signs of acute appendicitis. Severe neutropenia appeared to preclude conservative management and appendicectomy was performed. Though he was thrombocytopenic, bleeding was not troublesome at operation. Pathological examination showed a haemorrhagic appendix with no features of appendicitis.

Case 2.—A woman of 48 with acute myelomonocytic leukaemia in relapse developed severe abdominal pain. Several surgeons considered her to have acute appendicitis. Because of neutropenia, with its attendant risk of septicaemia and persistent severe pain, laparotomy was performed. Despite thrombocytopenic bleeding at operation was not marked. Laparotomy showed a normal appendix and a haematoma of the caecal wall. The abdomen was closed. She had no further abdominal pain—a finding which though never explained was gratefully accepted.

Case 3.—A man of 21 with acute lymphoblastic leukaemia in early relapse developed pain beneath the right costal margin accompanied by jaundice which was biochemically obstructive in nature. Increasing jaundice and the appearance of a palpable gall bladder prompted laparatomy, with the provisional diagnosis of biliary calculus or obstruction of the common bile duct by enlarged lymph nodes. At operation the gall bladder and bile ducts were grossly thickened by diffuse leukaemic infiltrates. No calculi or enlarged nodes were found. Postoperatively a further remission of his leukaemia was induced with prednisolone and the jaundice rapidly resolved.

Case 4.—A woman of 21 with acute myelomonocytic leukaemia was admitted to hospital with peripheral circulatory failure, oliguria, and severe abdominal pain. Her abdomen was distended and tympanitic and bowel sounds were much reduced. She was neither neutropenic nor thrombocytopenic and had not had any antileukaemic drugs for 10 days. An abdominal catastrophe of uncertain nature was diagnosed and laparotomy was planned. Despite vigorous attempts at resuscitation she deteriorated rapidly and died before operation could be performed. Careful necropsy disclosed no cause of death and, in particular, no abdominal abnormality other than some gaseous distension of small and large bowel with no physical obstruction.

In each of these cases the decision to operate was taken reluctantly and after much discussion, and even in retrospect these decisions seem to have been appropriate. Nevertheless, in no case was the preoperative diagnosis correct, and the three laparotomies actually performed were of little or no direct benefit to the patients.

Minor Procedures under General Anaesthesia

The investigation and treatment of leukaemia often involves minor but unpleasant procedures—bone marrow aspiration, trephine biopsy of the bone marrow, lumbar puncture, percutaneous puncture of the subclavian vein, aspiration of lymph nodes, dental extractions. In phlegmatic patients with high pain thresholds such procedures are often accomplished with local anaesthesia. With nervous patients and those with low pain thresholds, including children, the tendency is to use either sedation or systemic analgesics or both for these manœuvres, but this approach is often unsatisfactory. Sedation is seen mainly after the procedure, while the trauma of the process itself is not averted. Frequently a much etter course is to administer a brief general anaesthetic and perform several necessary procedures at the one time. For example, a child is given an inhalational anaesthetic (nitrous oxide and halothane) and has a bone marrow aspiration, lumbar puncture, intrathecal injection, and intravenous injections of cytotoxic drugs. Both parents and children find this technique acceptable ad non-traumatic. Evans *et al.*[13] had similar good results with outpatient anaesthesia in a children's leukaemia clinic, and the technique could well be more widely adopted.

Splenectomy in Leukaemia

ACUTE LEUKAEMIAS

Splenectomy has found no place in the current management of the acute leukaemias. Splenomegaly is almost never massive, and pancytopenia, if present, is due to bone marrow failure rather than hypersplenism. There is no evidence that splenectomy could do other than harm to the patient with acute leukaemia in relapse, while there seems no indication for this operation during remission. Indeed, some cases of acute lymphoblastic leukaemia can apparently be cured[5] by treatment regimens which do not include splenectomy. Possibly the spleen is of little importance in the natural history and therapeutic responsiveness of this acute leukaemia.

CHRONIC LYMPHOCYTIC LEUKAEMIA

Moderate or appreciable splenomegaly is not uncommon in chronic lymphocytic leukaemia and sometimes is inadequately controlled by cytotoxic drugs, steroids, or local irradiation. The splenomegaly is sometimes accompanied by pancytopenia, which itself may preclude further chemotherapy. Splenectomy may be recommended if (*a*) hypersplenism is shown—for example, excessive sequestration of isotopically labelled red cells or platelets or both in the enlarged spleen; or (*b*) studies of the bone marrow do not suggest advanced failure—for example, morphological preparations do not show total replacement by lymphocytes, and isotopic methods show significant iron utilization. Splenectomy can be expected to benefit most patients who satisfy these criteria, and for uncertain reasons the operation sometimes improves patients who do not. Thus istopic studies are a useful but by no means infallible guide.[14] Splenectomy is also indicated when chronic lymphocytic leukaemia is complicated by autoimmune haemolytic anaemia or autoimmune thrombocytopenia, which respond inadequately to

corticosteroid therapy. A good result can be expected in most patients.[15] Against the probable or possible benefits of splenectomy must be set the operative risks. Patients with chronic lymphocytic leukaemia are often elderly and frail, while both neutropenia and immunoglobulin deficiency render them prone to infection. The consensus of opinion appears to be that splenectomy can be a valuable measure in this disease, but the patients should be carefully selected. Both the quality of life and the ability to receive further antileukaemic chemotherapy can be improved.

CHRONIC GRANULOCYTIC LEUKAEMIA

Splenomegaly is almost invariable in chronic granulocytic leukaemia (C.G.L.) and is sometimes massive. The spleen is infiltrated with leukaemic cells which bear the same cytogenetic marker—the Philadelphia chromosome (Ph^1)—as the cells in the bone marrow.[21] Moreover, when the disease undergoes a malignant transformation to a rapidly progressive acute leukaemia multiple interrelated clones of leukaemic cells are detectable in the greatly enlarged spleen.[22] Experience of and opinions on splenectomy in C.G.L. vary widely. Early surgical series[23,24] did not suggest that the operation held any great promise; the mortality and morbidity in poorly selected cases were formidable, and progress in radiotherapy and chemotherapy did not encourage the surgical approach. Nevertheless, there is evidence that splenectomy can modify the natural history of C.G.L. In a previously untreated patient splenectomy was followed by eight months of haematological control of the disease without cytotoxic therapy.[25] Splenectomy in a patient who had received busulphan two years earlier was followed by three years of apparent remission of the C.G.L., with a six-year survival from operation.[26] Since the median survival in C.G.L. is only about 140 weeks[27] the achievement of six or more years of survival in a series of patients would represent a substantial gain.

Meeker *et al.*[28] splenectomized 15 patients with C.G.L.; apparently all the patients had either hypersplenism or symptomatic splenomegaly or both, and all but one had had C.G.L. for over a year before splenectomy. There were three operative deaths and eight patients improved haematologically after splenectomy. In four of these prolonged haematological control was achieved. At the time of publication of their report three patients were still alive at two, five, and nine years after the splenectomy. These workers later stressed[29] that their high operative mortality and morbidity seemed attributable to the relatively advanced disease in their patients. Since splenectomy nevertheless benefited patients with C.G.L. they felt that it should be considered earlier in the course of the disease. The relatively uncommon complication of thrombocytopenia occurring while C.G.L. is still in its chronic phase responds very well to splenectomy.[30] A recent report by French workers[31] suggests that splenectomy leads to some prolongation of survival in patients with C.G.L. In addition previously splenectomized patients survived longer than usual after their C.G.L. had transformed to an acute phase. Though three of the 18 patients splenectomized at Villejuif died of infection we have had no problems with postoperative sepsis in 17 of our own patients with C.G.L. who underwent splenectomy.

Neither Strumia *et al.*[17] nor Holt and Witts[16] considered that splenectomy produced satisfactory results in C.G.L. In a recent review of splenectomy in blood disorders[15] C.G.L. does not figure in the list of indications or in that of contraindications. Crosby's opinion, however, regarding splenectomy in Hodgkin's disease with hypersplenism—"Splenectomy should be done when the patient does not need it . . . if one waits until the patient needs the operation he may not be able to tolerate it"—might well be applied to splenectomy in C.G.L.

The following empirical reasons can be advanced for elective splenectomy early in the course of C.G.L.

(*a*) Late in the disease serious splenic problems are very common. These include pain, anorexia, wasting, infarction, rupture, haemorrhage, hypersplenism, and massive splenic blood pooling.

(*b*) Splenectomy at this time is hazardous, since the patient is ill and wasted, often thrombocytopenic and neutropenic, and has a massive spleen, often with adhesions.

(*c*) Nevertheless, splenectomy late in the course of C.G.L. can lead to improvement, with increased comfort, weight gain, an improved blood picture, and decreased transfusion needs.

(*d*) C.G.L. which has undergone metamorphosis to an acute leukaemia is less difficult to manage in the splenectomized patient because symptoms and bleeding are less and transfused blood and platelets are effective for longer periods.

(*e*) Though splenectomy is hazardous late in the course of C.G.L., and particularly so after metamorphosis has occurred, it is a simpler undertaking at a much earlier stage. Most patients are eligible because their disease is controlled, their spleens are small, and they are well, with a normal preoperative blood picture.

Thus there seems a good case for early splenectomy in C.G.L. as a prophylaxis against the almost inevitable splenic problems which will otherwise develop and decrease both the quality and the length of the patient's life.

Theoretical reasons may also be adduced which prompt early splenectomy in C.G.L. Survival in C.G.L. is limited by the transition of the disease into a refractory state, often resembling an acute leukaemia. This process has been likened to the metamorphosis of a conditioned neoplasm to an autonomous one.[32] The modest improvement in survival in C.G.L. which has occurred in the past 50 years appears to be due to a slight postponement of metamorphosis, probably as a consequence of close control of the total mass of leukaemic tissue during the chronic phase of the disease; regimens which achieve less close control result in shorter survival.[27] Splenectomy is an excellent way of reducing the body burden of leukaemic tissue, with less exposure to antileukaemic drugs, which may themselves adversely affect the evolution of the disease.[4] Furthermore, the spleen itself may represent a special site for the evolution of new and more anaplastic clones of cells which lead to the acute phase of C.G.L. Thus refractory splenomegaly is often the earliest sign of metamorphosis. Possibly also the spleen is a "pharmacological hideout" where leukaemic cells are protected from the effects of antileukaemic drugs; even very vigorous treatment for C.G.L. in metamorphosis rarely succeeds in abolishing the characteristic gross splenomegaly.

A controlled trial is needed to evaluate the effects of early elective splenectomy in C.G.L. The older series provide no conclusive information, since most of the operations were performed for indications such as hypersplenism, often in the presence of poorly controlled disease, and usually in cases diagnosed two or more years previously. A pilot study of elcetive splenectomy early in the course of C.G.L. was begun several years ago,[33] and results to date support both the feasibility and desirability of a larger cooperative study. The Medical Research Council's Working Party on Leukaemia in Adults has now instituted a multicentre controlled trial to study the effects of splenectomy on the duration and quality of survival in patients with C.G.L. Because of the rarity and chronicity of the disease it will require several years to obtain a conclusive result.

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Contemporary Themes

Horse-play: Survey of Accidents with Horses

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Summary

Horse-riding is increasing in popularity. During 1971 and 1972 154 patients had horse-related injuries of sufficient severity to warrant admission to the Radcliffe Infirmary. The injuries sustained are more common and more severe than generally appreciated and are comparable to those sustained by motor-cyclists. Supervision of children is often insufficient and protective leg and head gear is commonly quite inadequate, even when worn.

Introduction

Horse-riding is a common pursuit in the area served by the Accident Service of the Radcliffe Infirmary, Oxford, both as a hobby and professionally. The area has a population of about 450,000 and there are an estimated 3,000 to 4,000 horses used for riding. With the increase in popularity of the sport it was felt that the risk and the injury pattern should be clarified. This survey is of persons who received hospital inpatient treatment in 1971 and 1972 for injuries sustained in connexion with horses. Patients treated solely as outpatients are not included. During the two-year period 8,768 patients were admitted to the accident service and 154 had horse-related injuries. Total inpatient time for the 154 patients was 614 days. That is, one bed was almost constantly occupied by a victim of such an accident.

The distribution of patients according to age and sex is shown in fig. 1. A high proportion of patients were teenagers, with 90 patients under 21 years of age. Two-thirds (109) of the patients were female, and fig. 1 shows that teenage girls constituted one-third of all admissions. There was a clearly increased admission rate for both sexes during March to October, with a marked peak of female patients in July (fig. 2).

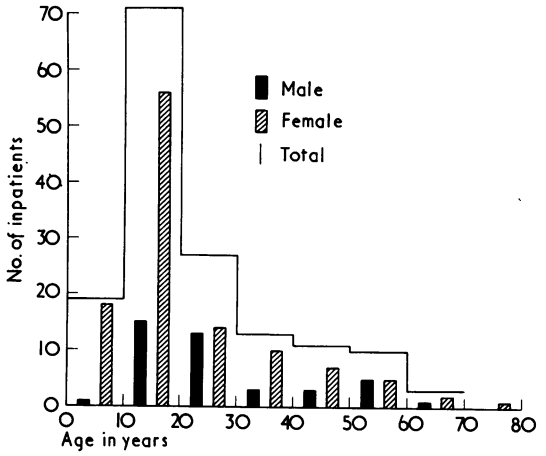

FIG. 1—Distribution of inpatients in 1971 and 1972 according to age and sex.

Thirty-six patients were professionally employed in their dealings with horses. These were predominantly stable lads, grooms, and jockeys, though farmers are also included in this figure.

Nature of Accident and Pattern of Injury

Most of the accidents (131) were to riders. Except for one girl who struck her head on a branch all were falls and the injury was due either to the fall itself or to being rolled on, kicked, or trodden on with the fall. Of the non-riders 13 patients were

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